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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Ballard Spahr LLP
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EXAMINER	
KIM, TAEYOON	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,417	MARCHASE ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *7-9,13-23 and 27-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-12 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-26), and PUGNAc and ischemia as elected species in the reply filed on 12/21/2009 is acknowledged. Applicant alleges that there would be no burden on the examiner in examining all of the claims at once. As indicated by applicant, the instant application is filed as the National Stage under 35 U.S.C. 371, and search burden is not a consideration in a finding of lack of inventive unity. As discussed in the previous OA, the current application discloses multiple methods/processes.

37 C.F.R. 1.475(d) states;

"If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims"

Therefore, Group I and Group II invention, both directed to the uses of a composition increasing concentration of an intracellular metabolite of a hexosamine biosynthetic pathway, are considered to lack unity of invention.

Applicant also argued that PCT International Search Report did not require restriction. On the international level, all written opinions are nonbinding and a patent does not issue; what does issue is an international preliminary examination report (IPER), which is nonbinding on the Elected States. See M.P.E.P. § 1878.01, Item V.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-9, 13-23 and 27-48 are withdrawn from consideration as being drawn to non-elected subject matter. Claims 1-6, 10-12 and 24-26 have been considered on the merits.

Information Disclosure Statement

The information disclosure statement filed 6/29/2007 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because there are no copy corresponding for two non-patent literature (designated as A31 and A32 in IDS) submitted. While there are two references without any number or date submitted, and they appears to be NIH R01 grant applications, however, there is no information (Grant #, author and date) given on the IDS list or the references that these references are corresponding to the citations given in the IDS. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

Claim 6 is objected to because of the following informalities: It is more appropriate to amend "comprises" to "is." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 10, 11 and 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pathogenic effect caused by stress other than

deterioration of β-cell function and insulin resistance associated with type 2 diabetes, does not reasonably provide enablement for deterioration of β-cell function and insulin resistance associated with type 2 diabetes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The instant claims are directed to a method of reducing a pathogenic effect caused by stress in a subject by administering a composition that increases a concentration of an intermediate metabolite of a hexosamine biosynthetic pathway (HBP).

The claims are broadly directed to any pathogenic effect caused by stress.
The specification discloses the definition for the term "pathogenic effect" meaning "an impairment of the normal state of the living cell, tissue, organ, recipient, or subject, or one of its parts, that interrupts or modifies the performance of one or more vital functions."

Kaneto et al. (J. Biol. Chem., 2001) teach that activation of the hexosamine pathway leads to deterioration of pancreatic β-cell function through the induction of oxidative stress, and leading to insulin resistance (Abstract).

Based on the teaching of Kaneto et al., it is expected that the activation of HBP leads increased stress (i.e. oxidative stress) causing pathological effect (i.e. deterioration of pancreatic β-cell and insulin resistance).

The teaching of Kaneto el al. shows an opposite effect of HBP activation causing stress and leading to deterioration of pancreatic β-cell function and insulin resistance.

Furthermore, Kudlow et al. (US 2003/0186948) teach that PUGNAc, an inhibitor, is another diabetogenic chemical inhibitor of O-N-acetyl glucosaminease (O-GlcNAcase) as

streptozotocin (par. 97). Since PUGNAc is considered as diabetogenic, and considering diabetic conditions (deterioration of pancreatic b-cells and insulin resistance as taught by Kaneto et al.) being associated with oxidative stress, the use of PUGNAc, inhibitor of O-GlcNAcase, contradicts the claimed effect of reducing a pathogenic effect caused by stress.

Therefore, it is considered that the specification does not enable the entire scope of the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 10-12, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. (WO2002/067949; for English translation, US Pat. 7,074,774 was relied on).

Xu et al. teach a method of treating or preventing cardiac and cerebral ischemia (which is considered not associated with a hyperactivated inflammatory response) and oxygen-deficiency by administering to a patient in need thereof an effective amount of N-acetyl-D-glucosamine (N-acetylglucosamine) (see abstract and col.2, lines 3-14).

Xu et al. do not teach the limitation directed to the effect of the claimed composition to increase a concentration of an intracellular metabolite of a hexosamine biosynthetic pathway (HBP) (claim 1), or the increase in the concentration of the intracellular metabolite to inhibit cellular calcium overload (claim 3) or the intracellular metabolite of HBP being uridine diphosphate-N-acetylglucosamine (UDP-GlcNAc) (claim 4).

However, these limitations do not require any active step to be carried out for the claimed method steps, rather they merely state the result of the limitations (method steps) in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.,* 57 USPQ2d 1747 (Fed. Cir. 2001).

The discovery of a new use for an old structure based on unknown properties of the structure *might* be patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). However, when the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated. *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978) and *In re Tomlinson*, 363 F.2d 928, 150 USPQ 623 (CCPA 1966). See M.P.E.P. § 2112.02.

While Xu et al. do not teach the claimed effect related to HBP, they do perform the same method steps of administering N-acetylglucosamine (N-GlcNAc) as in the present application (p.18, line 20; withdrawn claim 7). Because the method steps of Xu et al. are the same and thus inherently teach the same process of increasing intracellular metabolites of a HBP, inhibiting cellular calcium overload or the increased intracellular metabolite being UDP-GlcNAc as in the current application. Xu et al. therefore anticipate the claimed effect as instantly claimed.

Xu et al. teach that the administration of N-acetyl-D-glucosamine being before the carotid artery of rat being clamped (col. 4, lines 1-3), which meet the limitation of administering prior to the stress as in claim 11. Furthermore, the method of Xu et al. is also for treating a

subject having a cardiac or cerebral ischemia (col. 6, lines 13-17), satisfying the limitation of during or after the stress.

Xu et al. teach the method being administered/applied to animals and human (col. 2, lines 63 through col.3, line 3), meeting the limitations of claims 25 and 26.

Thus, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 10-12 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. (supra).

Xu et al. anticipate the claimed subject matter of claims 1-4, 10-12, 25 and 26, and thus render them obvious (see above).

Xu et al. do not particularly teach the composition being administered over a period from about 5 min. to about 1 hour (claim 24).

However, it is considered that the duration of administering the composition is a variable which achieves a recognized result, thus, a result-effective variable, and the determination or workable ranges of the variable would be characterized as routine experimentation.

It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re* Aller, Lacey, and Haft, 105 USPQ 233 (CCPA 1955): Normally, it is to be expected that

a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. *In re* Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931,24 USPQ 52; *In re* Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. *In re* Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; *In re* Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. *In re* Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; *In re* Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; *In re* Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re* Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11,57 USPQ 136. (Emphasis added). With regards to determining experimental parameters, such as time in culture, the court has held that "[d]iscovery of optimum value of result effective variable in known process is ordinarily within skill of art (In re Boesch and Slaney, 205 USPQ 215 (CCPA 1980)).

The adjustment of particular conventional working conditions is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan having the cited reference before him/her.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651